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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/421,971 | 10/20/1999 | FRED H. GAGE | SALK2350 | 4863 |

7590 12/24/2003

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| EXAMINER | |
|---|---|
| MURPHY, JOSEPH F | |

| ART UNIT | PAPER NUMBER |
|---|---|
| 1646 | |

DATE MAILED: 12/24/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/421,971 | GAGE ET AL. | |
| | Examiner | Art Unit | |
| | Joseph F Murphy | 1646 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *04 September 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *1-11 and 13-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-11 and 13-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. §§ 119 and 120**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☒ Interview Summary (PTO-413) Paper No(s). *12182003*.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

## DETAILED ACTION

### *Formal Matters*

Claims 1-11, 13-22 are pending and under consideration. The finality of the last Office action is withdrawn, and new grounds of rejection are set forth below.

### *Response to Amendment*

The rejection of claims 1-5, 14, 19, 22 under 35 U.S.C. 102(e) as being anticipated by U.S. Patent No. 5,830,462 (Crabtree et al.) has been withdrawn.

The rejection of claims 1-1 1, 13-14, 19-22 under 35 U.S.C. 103(a) as being unpatentable over U.S. Patent No. 5,830,462 (Crabtree et al.) in view of U.S. Patent No. 6,265,173 (Evans et al.) has been withdrawn.

### *Claim Rejections - 35 USC § 112 first paragraph*

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-11, 13-22 are rejected under 35 U.S.C. 112, first paragraph, because the specification, which is enabling for a chimeric protein comprising a fusion of EcR-USP/RXR into a functional dimer, does not reasonably provide enablement for chimeric proteins comprising two functional protein units wherein each functional protein unit comprises the dimerization domain of a member of the steroid/thyroid hormone nuclear receptor superfamily. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Claims 1-11, 13-22 are overly broad since they encompass functional dimers comprising any member of the steroid/thyroid hormone nuclear receptor superfamily, which are set forth on page 13 line 19 to page 14, line 23 of the specification. The claims thus encompass dimers comprising, inter alia, glucocorticoid receptors, mineralocorticoid receptors, estrogen receptor, progesterone receptor, androgen receptor, vitamin d3 receptor, retinoic acid receptors, farnesoid X receptors etc., as well as members of this superfamily from any animal. Applicant has provided an example wherein a chimeric protein comprising a fusion of EcR-USP/RXR into a functional dimer was made. However, the art recognizes that the nuclear hormone receptor superfamily is a large and complex family, (see Aranda A, Pascual A. Nuclear hormone receptors and gene expression. Physiol Rev. 2001 Jul;81(3):1269-304). The Aranda reference teaches that the exact biochemical mechanisms by which these receptors stimulate transcription are still unclear (page 1296, first column). The Aranda reference further teaches that the superfamily is subdivided into six distinct subfamilies (page 1271, column 1, fourth paragraph). The Aranda reference further teaches that there are functional differences within the superfamily, for example, the receptors can bind as monomers, homodimers or heterodimers see page 1275, column 2, first and second paragraphs. Furthermore, the claims encompass members of the superfamily that are orphan receptors, for which no ligand is known (page 1272, Table 1). The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue. See In re Wands, 858 F.2d at 737, 8 USPQ2d at 1404. While the claims set forth a functional limitation for the chimeric polypeptides wherein the polypeptide can bind DNA, bind ligand, transactivate or dimerize, as taught by the Aranda reference, the exact biochemical mechanisms by which these receptors stimulate transcription are

still unclear, and additionally, the encompassed proteins differ in the function, in that some form dimers, while some function as monomers. Furthermore, since the ligand for many of the encompassed protein are unknown, one of skill in the art would not be able to test for the ligand binding function. Since detailed information regarding the structural and functional requirements of the polypeptide are lacking, it is unpredictable as to which of the encompassed proteins, if any, meet the limitations of the claims. Applicant is required to enable one of skill in the art to make and use the claimed invention, while the claims encompass polypeptides that the specification only teaches one skilled in the art to test for functional variants. It would require undue experimentation for one of skill in the art to make and use the claimed polypeptides. Since the claims do not enable one of skill in the art to make and use the claimed polypeptides, but only teaches how to screen for the claimed polypeptides, and since detailed information regarding the structural and functional requirements of the polypeptides are lacking, it is unpredictable as to which variations, if any, meet the limitations of the claims. Thus, since Applicant has only taught how to test for chimeric proteins comprising two functional protein units wherein each functional protein unit comprises the dimerization domain of a member of the steroid/thyroid hormone nuclear receptor superfamily, and has not taught how to make chimeric proteins comprising two functional protein units wherein each functional protein unit comprises the dimerization domain of a member of the steroid/thyroid hormone nuclear receptor superfamily, it would require undue experimentation of one of skill in the art to make and use the claimed polypeptides.

Claims 1-11, 13-22 are rejected, under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 66, No. 4, pages 1099-1111, Friday January 5, 2001.

These are genus claims. The claims encompass functional dimers comprising any member of the steroid/thyroid hormone nuclear receptor superfamily, which are set forth on page 13 line 19 to page 14, line 23 of the specification. The claims thus encompass dimers comprising, inter alia, glucocorticoid receptors, mineralocorticoid receptors, estrogen receptor, progesterone receptor, androgen receptor, vitamin d3 receptor, retinoic acid receptors, farnesoid X receptors etc., as well as members of this superfamily from any animal. The specification and claims do not indicate what distinguishing attributes shared by the members of the genus. The scope of the claim includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claim do not provide sufficient guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a chimeric protein comprising a fusion of EcR-USP/RXR

functional dimer is insufficient to describe the genus. The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus of polypeptides. There is no description of the conserved regions which are critical to the structure and function of the genus claimed. There is no description of the sites at which variability may be tolerated and there is no information regarding the relation of structure to function. Structural features that could distinguish the compounds in the genus from other seven transmembrane region compounds are missing from the disclosure. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the polypeptides encompassed (see see Aranda A, Pascual A. Nuclear hormone receptors and gene expression. Physiol Rev. 2001 Jul;81(3):1269-304). The Aranda reference teaches that the exact biochemical mechanisms by which these receptors stimulate transcription are still unclear (page 1296, first column). The Aranda reference further teaches that there are functional differences within the superfamily, for example, the receptors can bind as monomers, homodimers or heterodimers see page 1275, column 2, first and second paragraphs. Furthermore, the claims encompass members of the superfamily that are orphan receptors, for which no ligand is known (page 1272, Table 1). Thus, no identifying

characteristics or properties of the instant polypeptides are provided such that one of skill would be able to predictably identify the encompassed molecules as being identical to those instantly claimed. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus, thus, applicant was not in possession of the claimed genus.

***Conclusion***

No claim is allowed.

***Advisory Information***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
December 22, 2003